

What Is Claimed Is:

1. A method for identifying an individual who has an altered risk for developing Alzheimer's disease, comprising detecting a single nucleotide polymorphism (SNP) in any one of the nucleotide sequences of SEQ ID NOS:1-433 and 867-54,769 in said individual's nucleic acids, wherein the presence of the SNP is correlated with an altered risk for Alzheimer's disease in said individual.
2. The method of claim 1 in which the altered risk is an increased risk.
3. The method of claim 2 in which said individual has Alzheimer's disease.
4. The method of claim 1 in which the altered risk is a decreased risk.
5. The method of claim 1, wherein the SNP is selected from the group consisting of the SNPs set forth in Tables 6 and 7.
6. The method of claim 1 in which detection is carried out by a process selected from the group consisting of: allele-specific probe hybridization, allele-specific primer extension, allele-specific amplification, sequencing, 5' nuclease digestion, molecular beacon assay, oligonucleotide ligation assay, size analysis, and single-stranded conformation polymorphism.
7. An isolated nucleic acid molecule comprising at least 8 contiguous nucleotides wherein one of the nucleotides is a single nucleotide polymorphism (SNP) selected from any one of the nucleotide sequences in SEQ ID NOS:1-433 and 867-54,769, or a complement thereof.
8. The isolated nucleic acid molecule of claim 7, wherein the SNP is selected from the group consisting of the SNPs set forth in Tables 3 and 4.
9. An isolated nucleic acid molecule that encodes any one of the amino acid sequences in SEQ ID NOS:434-866.
10. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:434-866.
11. An antibody that specifically binds to a polypeptide of claim 10, or an antigen-binding fragment thereof.
12. The antibody of claim 11 in which the antibody is a monoclonal antibody.

13. An amplified polynucleotide containing a single nucleotide polymorphism (SNP) selected from any one of the nucleotide sequences of SEQ ID NOS:1-433 and 867-54,769, or a complement thereof, wherein the amplified polynucleotide is between about 16 and about 1,000 nucleotides in length.

5 14. The amplified polynucleotide of claim 13 in which the nucleotide sequence comprises any one of the nucleotide sequences of SEQ ID NOS:1-433 and 867-54,769.

10 15. An isolated polynucleotide which specifically hybridizes to a nucleic acid molecule containing a single nucleotide polymorphism (SNP) in any one of the nucleotide sequences in SEQ ID NOS:1-433 and 867-54,769.

16. The polynucleotide of claim 15 which is 8-70 nucleotides in length.

17. The polynucleotide of claim 15 which is an allele-specific probe.

18. The polynucleotide of claim 15 which is an allele-specific primer.

15 19. The polynucleotide of claim 15, wherein the polynucleotide comprises a nucleotide sequence selected from the group consisting of the primer sequences set forth in Table 5 (SEQ ID NOS:54,770-55,342).

20. A kit for detecting a single nucleotide polymorphism (SNP) in a nucleic acid, comprising the polynucleotide of claim 15, a buffer, and an enzyme.

20 21. A method of detecting a single nucleotide polymorphism (SNP) in a nucleic acid molecule, comprising contacting a test sample with a reagent which specifically hybridizes to a SNP in any one of the nucleotide sequences of SEQ ID NOS:1-433 and 867-54,769 under stringent hybridization conditions, and detecting the formation of a hybridized duplex.

25 22. The method of claim 21 in which detection is carried out by a process selected from the group consisting of: allele-specific probe hybridization, allele-specific primer extension, allele-specific amplification, sequencing, 5' nuclease digestion, molecular beacon assay, oligonucleotide ligation assay, size analysis, and single-stranded conformation polymorphism.

30 23. A method of detecting a variant polypeptide, comprising contacting a reagent with a variant polypeptide encoded by a single nucleotide polymorphism (SNP)

in any one of the nucleotide sequences of SEQ ID NOS:1-433 and 867-54,769 in a test sample, and detecting the binding of the reagent to the polypeptide.

24. A method for identifying an agent useful in therapeutically or prophylactically treating Alzheimer's disease, comprising contacting the polypeptide of claim 10 with a candidate agent under conditions suitable to allow formation of a binding complex between the polypeptide and the candidate agent, and detecting the formation of the binding complex, wherein the presence of the complex identifies said agent.

25. A method for treating neurodegenerative disease in a human subject, which method comprises administering to said human subject a therapeutically or prophylactically effective amount of an agent which inhibits the activity of glyceraldehyde-3-phosphate dehydrogenase.

26. A method for treating neurodegenerative disease in a human subject wherein said human subject harbors a mutant glyceraldehyde-3-phosphate dehydrogenase (GAPDH) gene, which method comprises administering to said human subject a therapeutically or prophylactically effective amount of an agent counteracting the neurodegenerative effects of the disease.

27. The method of Claim 26 in which the agent is neuroprotective.

28. The method of Claim 27 in which the agent is anti-apoptotic.

29. The method of Claim 28 in which the agent inhibits the activity of GAPDH.

30. The method of Claim 29 in which the agent inhibits the activity of GAPDH by forming a binding complex with GAPDH.

31. The method of Claim 30 in which the disease is selected from adrenoleukodystrophy, Alexander Disease, Alzheimer's disease, amyotrophic lateral sclerosis, Canavan Disease, cerebellar degeneration, cerebral ischemias, glaucoma, Krabbe Disease, metachromatic leukodystrophy, multiple sclerosis, neuronal ceroid lipofuscinoses, Parkinson's disease, Pelizaeus-Merzbacher Disease, retinitis pigmentosa, stroke, neurodegenerative disease caused by traumatic injury.

32. The method of Claim 29 in which the mutant GAPDH gene comprises a polynucleotide sequence selected from the group consisting of the genomic sequence of SEQ ID NO:6795, the transcript sequences of SEQ ID NOS:125-127, and nucleic acid

sequences that encode a polypeptide comprising an amino acid sequence of SEQ ID NOS:558-560.

33. The method of Claim 25 in which the agent is selected from (*R*)-*N*-methyl-*N*-(1-methyl-2-phenyl-ethyl)-*N*-prop-2-ynylamine, dibenzo[*b,f*]oxepin-10-ylmethyl-
5 methyl-prop-2-ynyl-amine and (*R*)-indan-1-yl-prop-2-ynyl-amine.

34. A method for identifying an agent useful in therapeutically or prophylactically treating neurodegenerative disease in a human subject wherein said human subject harbors a mutant glyceraldehyde-3-phosphate dehydrogenase (GAPDH) gene, which method comprises contacting GAPDH with a candidate agent under
10 conditions suitable to allow formation of a binding complex between the GAPDH and the candidate agent and detecting the formation of the binding complex, wherein the presence of the complex identifies said agent.

35. A method for treating neurodegenerative disease in a human subject wherein said human subject harbors a mutant glyceraldehydes-3-phosphate
15 dehydrogenase (GAPDH) gene, which method comprises:

- (i) determining that said human subject harbors the mutant GAPDH gene; and
- (ii) administering to said subject a therapeutically or prophylactically effective amount of one or more agents counteracting the neurodegenerative effects of the disease.